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## THE HISTOLOGICAL LESIONS PRODUCED BY THE TOX-ALBUMEN OF DIPHTHERIA.


BY WM. H. WELCH, M. D., *Professor of Pathology*, AND SIMON FLEXNER, M. D., *Fellow in Pathology.*

(*From the Pathological Laboratory of the Johns Hopkins Hospital and University.*)


In a preliminary communication presented to the Johns Hopkins Hospital Medical Society, and published in the HOSPITAL BULLETIN, No. 15, August, 1891, we called attention to the histological changes in the organs of animals which had died of experimental diphtheria, following the inoculation of pure cultures of the bacillus diphtheriæ. Since then we have extended our investigations so as to include the study of the lesions produced by the inoculation of the toxic products of the diphtheria bacillus. This study virtually finishes the work we have undertaken, and it is hoped soon to publish our results in detail. However, in order to make our preliminary communication complete, we append this report.

The toxic products of the diphtheria bacillus with which we have operated were obtained by filtering through a new and sterilized Chamberland filter a culture of the organisms in glycerine-bouillon several weeks old. The fluid so obtained was tested by means of cover-slips and inoculations on glycerine-agar, and proved to be sterile.

Guinea-pigs were used for the experimental inoculations. The sterile culture fluid was introduced subcutaneously into the tissues of the belly-wall. The method pursued will be given in connection with the case of which the lesions are to described. This guinea-pig received on the 10th of December, 1891, 1 cc. of the filtrate. Not having succumbed, on December 14th it received 2 cc. more. The animal died on January 5th, 1892, the duration of life since the first inoculation having been three weeks and five days, and since the last, three weeks and one day.

At the autopsy the vessels of the subcutaneous tissues were injected, and hemorrhage had taken place into the tissues of the axillary and inguinal regions. The subcutaneous tissues were moist, but there was no actual œdema present. Neither was there a visible area of localized inflammation. There was no microscopical examination made, however. The lymphatic glands of the axillary and inguinal regions were enlarged and reddened; the cervical lymph glands were swollen, and the thyroid gland was greatly congested.

There was a considerable excess of clear fluid in the peritoneal cavity. Both layers of the peritoneum were reddened, the vessels of the visceral layer being especially injected. The spleen was enlarged to double the average size. It was mottled, and the white follicles were distinctly outlined against the red ground. The liver was dark in color and contained much blood. On the surface a prominent yellowish-white area 2 mm. in diameter, surrounded by a zone of hyperæmia, was observed. Smaller dot-like points of the same color and general appearance were seen elsewhere in the liver. The kidneys were congested and the cut surface was cloudy. The adrenal glands appeared normal, as did the mesenteric glands.

The pleural cavity did not contain such a marked excess of fluid. The pericardial sac, however, was distended with clear serum. Under the epicardium were many ecchymotic spots.

The lungs exhibited areas of intense congestion, or actual hemorrhage into the tissues. The glands of the thorax were, perhaps, swollen.

The examination of frozen sections showed the heart muscle to be slightly fatty. The epithelium of the tubules of the kidney was extremely granular and much swollen, but not fatty. The liver was very fatty; the lighter areas and dots were seen to correspond to foci of dead liver cells, whose refraction was much greater than that of the normal cells.

Cultures were made from the blood and organs of the animal and they remained sterile. Cover-slips were also examined and no organisms found.

The histological lesions observed in this case are identical with those described by us in connection with the inoculation of the living organisms. Lymphatic apparatus: In general, the changes are the same throughout. They are found in the greatest intensity in the glands of the axillary and inguinal regions, and less in the bronchial, cervical, mediastinal and mesenteric glands. Yet these are considerably affected. The same fragmentation of nuclei, affecting the lymph nodes and sinuses, is met with. These fragments exhibit the variety of form previously described by us, and they have the same affinity for coloring agents. Much of the nuclear detritus is free, but a part is contained within large pale cells. In the spleen there is a similar diffuse fragmentation of the nuclei of the spleen cells. Both the lymphoid cells of the follicles and the larger cells of the sinuses are affected. Like the lymphatic glands, some of the nuclear detritus is enclosed in large cells. Besides the destruction of cells in the spleen there is hemorrhage into the organ, or an extreme degree of congestion, so that the tissue elements are widely separated from one another. Nuclear figures occur in the lymph glands and spleen. In the former they are found among the fragmented cells.

Stained sections of the liver, especially those stained in methylene-blue and eosine, show the yellowish-white areas to be composed of hyaline, necrotic liver cells. The necrotic cells stain deeply in the eosine, and they are usually devoid of nuclei. They form, on the whole, more or less definite foci of hyaline cells into which leucocytes have wandered. The largest area was 2 mm. in diameter, and the outlines of it were formed by hemorrhage into the tissues, corresponding with the hyperæmic zone spoken of above. The cells in this focus have lost their nuclei and they are intensely refractive. Many of the dead cells have retained their individuality, and, indeed, their borders are more distinct than those of the normal cells. Others, however, tend to become fused together and to lose their individual cell outlines. Occasionally, outside the main focus of hyaline cells, single necrotic cells occur which are surrounded by quite normal ones. Many leucocytes have wandered into this area of dead cells, and they are especially abundant at one place in the focus in which the hyaline and necrotic cells are in process of disintegration. An exquisite nuclear fragmentation is to be observed throughout this area.

Should the focus just described be compared to many similar foci which occur in the livers of animals dead of inoculation with the bacilli themselves, it will be seen to contain more leucocytes (polynuclear) within it. The explanation of this fact would seem to depend somewhat on the incubation time, but more on the progression or stage of the necrotic process. Inoculation of the bacilli usually leads to death in a very short time, often in 24 to 48 hours. In this inoculation with the toxic products alone, the incubation period exceeded three weeks. On account of this, time has been allowed for the softening and disintegration of the dead cells, and leucocytes have been strongly attracted to these foci.

In the kidneys, besides the condition described in the frozen sections, a slight fragmentation of the nuclei of the epithelium of the tubules is encountered. The lungs exhibit areas of hemorrhage into the alveoli, and in many of these there has been a desquamation of the alveolar epithelium. Sometimes the desquamated epithelial cells are quite normal in appearance, while at others they have fragmented nuclei. The collections of lymphoid cells around the medium-sized and larger bronchi show, however, more cells, the nuclei of which have suffered in this way.

The blood-vessels of the tissues generally contain fewer leucocytes in this instance than in those cases in which the bacilli were introduced beneath the skin. By the latter method an intense local inflammatory process is provoked, associated with the emigration of large numbers of polynuclear leucocytes. In the former, in which the filtrate, free from organisms, is used for inoculation, the local process is reduced to nil, there is no emigration of leucocytes, and the disease is general from its inception. This difference is sufficient to account for the occurrence of leucocytes in the one case and its absence in the other.

It may be considered as established now that the toxic products and not the bacilli themselves invade the tissues in diphtheria. This fact would at once suggest that the general lesions (those produced at a distance from the seat of inoculation in animals, and the situation of the local process in human beings) were the effects of the soluble poison diffused through the body. Hence, it was desirable to demonstrate this assumption experimentally; and it is not unimportant to know that the lesions in the tissues produced by the bacilli and the toxic principle on the one hand, and the toxic principle alone on the other, are in perfect correspondence with each other. And, moreover, it would seem not to be superfluous to emphasize the occurrence of definite focal lesions in the tissues of the body, produced by a soluble poison circulating in the blood.

# A SERIES OF FIFTY CONSECUTIVE OPERATIONS FOR CATARACT.

BY ROBERT L. RANDOLPH, M. D., *Assistant Ophthalmic and Aural Surgeon to the Johns Hopkins Hospital and Dispensary.*

*Read at a meeting of the Hospital Medical Society, Nov.* 2, 1891.

Statistics of operations for cataract are so numerous nowadays that little is left to be said beyond the mere tabular report. Nearly every surgeon, though, learns from his own particular experience something which is new and which is worth adding to the history of this operation.

As regards the operation with and without iridectomy, thus far I have seen no reason to abandon the iridectomy, though I confess that had the surroundings of my patients been such as the majority of cataract patients enjoy I would have practiced simple extraction more frequently. Few operators are in a position to put about their patients the comforts and safeguards that may be had in a hospital like this one or the Presbyterian Eye and Ear Hospital of this city. Out of the fifty operations here recorded six were performed in a hospital, namely, three in the Johns Hopkins Hospital and three in the Presbyterian Eye and Ear Hospital, and all did well. With the exception of eighteen, the remaining twenty-six were among the poorer classes of a country population of Virginia and in a mining region in the western part of this State. The first case reported here was operated upon in a log cabin near Warrenton, Virginia, and the old man was nursed by his daughter, who only saw him at mealtimes and at night. He was compelled, then, to help himself the greater part of the time, and as a consequence exposed himself to risks every hour of the day. He went through the same experience a year later, and, as in the first instance, he obtained excellent vision. Case 8 was a colored man 87 years old and blind for three years. He lived on the extreme end of my father's plantation in Virginia and was nursed by his wife. His cabin was too dark to perform an operation in with safety, and I put him on a cot and operated out in the yard. He was very timid, and jumped when I performed the iridectomy, causing some loss of vitreous. He counted my fingers after the operation, and I assisted him upstairs to a room next to the roof, as the only other room in the house opened out into the yard. He remained there for a week, and at the end of that time was allowed to come downstairs. He made an uneventful recovery, and subsequently obtained perfect vision with the proper glasses. Case 39 was operated upon in a cabin full of negro children and his daughter looked after him. The result was most satisfactory.

Home nursing at best is rarely comparable to good hospital nursing. The majority of these fifty cases were subjected to indifferent care and attention at the hands of, for the most part, ignorant persons, and among these twenty-six cases there were eighteen whom I did not see the second time till two weeks after the operation. Eight out of these eighteen had three visits a week from the family physician, and the remaining ten had absolutely no medical attention beyond what members of the family could give until I saw the patient two weeks after the operation. It is true, under these circumstances, I gave the most explicit directions to that member of the family to whose special care I would entrust my patient, but at best the after-treatment of this class of patients differed radically from what we see even in a general hospital where there are no special provisions for cataract patients. Among these fifty cases only two failed to recover sight, and as the circumstances peculiar to these two were rather unusual, and as such would probably explain the failure, I shall give the histories.

Case 49, woman 78 years old, had been troubled many years with dacryocystitis, more marked in the left eye than in the right. She had been blind from cataract for three years. Refused treatment for the lachrymal trouble, saying she was too weak and old to stand the pain incident upon the probing. She was made acquainted with the additional risk of a cataract operation performed on an eye when there was disease of the lachrymal sac. She was willing, however, to run the risk of infection from this source, so I operated on the least affected eye. The result was a perfect success. A year later she presented herself for operation upon the second eye. The operation was smooth and she counted fingers with ease immediately afterward. I left the city that evening, not expecting to see her again for two weeks. She was entrusted to the care of the physician who assisted me in the operation. It is well to state here that she belonged to a most ignorant class of white people, and though nearly eighty years of age, was accustomed to going barefooted in warm weather. The first time I operated she had shown herself unmanageable and walked around the house three days after the operation. That was in the winter time. The second operation was in June last, and when I saw the patient two weeks after the operation her physician told me that she got up out of bed the next day, tore the plaster off her good eye and came downstairs and sat in the yard and smoked her pipe. The second day after the operation she walked nearly a mile barefooted to see her daughter. Whatever were the causes which produced it, when I saw her the second time the eye was lost. It is impossible, then, to say whether to attribute the loss of the eye to infection from the mucocele or to carelessness and exposure after the operation. Before each operation the contents of the lachrymal sac were pressed out, and, as far as possible, the conjunctival sac was rendered aseptic by irrigating it with a solution of corrosive sublimate $\frac{1}{4000}$.

The second case (Case No. 47) is that of a man sixty-one years old. He had been subject for many years to rheumatism, and had suffered also for a long time with varicose veins on both legs, and as a result of the latter condition his right leg was covered with an eczema. The blood-vessels at his wrists and temples were tortuous and hard. Left eye, total cataract and good field of vision for light. The operation was as smooth as any I ever performed, and after the delivery of the lens the patient could see my face and count fingers readily. I removed the speculum and closed the eye, putting on the usual bandage. Ten minutes later, and just before I was about to leave the house, he complained of violent pain in the eye. I suspected hemorrhage and immediately removed the bandage to investigate. I found the latter soaked with

blood. The mass of blood and protruding vitreous were cleaned away and strong pressure applied. On returning six hours later it was found that the oozing had continued and he was still suffering pain. The lids were opened and a clot of vitreous was discovered between the edges of the wound. This was removed, and after first irrigating the conjunctival sac with a very weak sublimate solution, a pressure bandage was applied. At my visit the next day I found the bandage quite moist and there was every evidence that the oozing was persisting. I cleaned out the sac again and renewed the bandage. On the afternoon of the second day I saw him again and there were still signs of hemorrhage. The same course of treatment was pursued and on the third day I found the bandage clean. Of course he was told that vision was irrevocably gone from the onset of the hemorrhage. In nearly all cases of this class the cornea sloughs, but this termination I fortunately escaped. Hemorrhage after cataract extraction is rare. Dr. Knapp reports in a recent number of the Archives of Ophthalmology his only case. In my own case I can account for the hemorrhage only by the condition of the blood-vessels throughout his body. No doubt the vessels of the retina were tortuous and their walls atheromatous, and when the lens was removed and intraocular tension thereby lowered, the blood-vessel walls could not withstand the pressure from the increased volume of blood pouring into them, so they ruptured. The whole condition of the patient pointed to a diseased state of the circulatory apparatus. It is impossible to guard against such a termination, though I should regard it as a contra-indication for operation upon the other eye, for no matter how smooth the operation might be, the chances are that hemorrhage would follow the delivery of the lens.

In case No. 7, an old gentleman of 75 years, I allowed the patient, as is my custom, to get up out of bed the day after the operation. That afternoon I went to see him and found him fast asleep in a chair by an open window with only the shutters closed. A storm was coming up and it had been blowing violently for nearly an hour, and on entering the room I observed that the wind was blowing directly on his bald head, as the curtains were fluttering about his shoulders. He awoke as I entered and commenced to sneeze. I predicted trouble then and there, and sure enough iritis set in a few hours later. He was treated vigorously with sodium salicylate and instillations of atropia, and the inflammation subsided in three weeks, leaving him with almost a closed pupil and with very poor vision. Discission a year later gave him $\frac{20}{200}$ vision; in other words, the ultimate result was satisfactory.

This case was of special interest to me, inasmuch as it presented the rather unusual effect of large doses of salicylate of soda. About midnight, after taking during the day nearly 180 grains of the drug, he became delirious and imagined that some one was pursuing him. He tore up the sheets on his bed and took the bandage off his eye, and was found by the gentleman of the house sitting on the bare floor, raving in the wildest manner, and it was with the utmost difficulty that he could be induced to return to bed. I gave him a hypodermatic injection of morphia and discontinued the use of the salicylate of soda, and the mental trouble disappeared. I have since given even larger doses in the same length of time and have not seen this effect.

With regard to the method of operating. The instruments were allowed to remain twenty minutes in absolute alcohol, and I have found that this agent answered my purposes on the whole more satisfactorily than either carbolic acid, corrosive sublimate or hot water. I am, of course, aware that alcohol is inferior to either of the three above-named agents as a germicide, but, from the point of view of convenience, among the greater number of these fifty cases it has been found capable of a wider application. I should prefer boiling water as a sterilizing agent for routine hospital work, but frequently when it was asked for among several of my patients I would be brought boiling water, it is true, and no doubt free from micro-organisms, but full of sediment of all kinds and deposit from the sides of a dirty kettle. It is hard to prevent a drop or more of a carbolic acid solution from coming in contact with the eyeball when using this agent as a disinfectant for the instruments, and such a result is always followed by a decided hyperæmia, a condition always to be avoided. I have a tin box ten inches long and three inches wide and one inch deep, and within this a rack for all instruments needful for the occasion. The instruments are placed in the box and the latter is filled with alcohol. The instruments are taken out a couple of minutes before they are used, to allow any excess of the solution to evaporate from their sides, keeping the conjunctiva free from contact with an agent which in any way might irritate, and this is manifestly not possible to the same degree with any aqueous solution. I use a solution of $\frac{1}{1000}$ corrosive sublimate to wash the lids, but unless there be some good reason for it, as in troubles of the lachrymal sac, I never irrigate the conjunctiva with antiseptic agents of any kind whatever. Irrigations of corrosive sublimate, according to Knapp, have been known to stain the cornea indelibly, and I find that such irrigations, indeed irrigations of all kinds, produce more or less hyperæmia of the conjunctiva and so increase the liability of hemorrhage into the section. Beyond a two per cent solution of cocaine, to every ounce of which I have added ten grains of boric acid, I introduce nothing foreign between the eyelids. As regards the dressing, I still think the bandage the safer mode of procedure, and while it is far more uncomfortable than the plaster strip, it seems wiser to sacrifice comfort, indeed anything within reason, to increased security.

In simple extraction it seems to me that one would be more apt to get a round pupil by employing the bandage. My section is made in the clear cornea, with possibly a slight tendency to the conjunctiva. In the five simple extractions reported I have made the apex of the section well out into the clear cornea. Such a section, I think, lessens the probability of prolapse of the iris. In opening the capsule I split the latter horizontally and above, near the border of the lens. In the operations with iridectomy it has been my custom to instil a solution of atropia (4 grs. to ℥i) into the eye on the evening of the second day. In simple extraction a couple of drops of eserine (2 grs. to ℥i) are instilled immediately after the operation, and no further drops are used during the treatment

unless specially demanded. The unoperated eye is always kept closed by a strip of adhesive plaster, which is removed on the evening of the second day. This is done simply to keep the eyeballs still as far as possible until the corneal wound has united. The patients are required to remain quiet in bed (or at least lying down) for twelve hours after the operation. It is my object to keep the patients guarded against direct rays of light, so the room is simply shaded with that view, but is never so dark that one would be unable to see to read. As regards diet there is absolutely no restriction. The bandage is removed on the sixth day, and after this atropia is instilled regularly (in the iridectomy cases) twice daily till the fourteenth day.

If we arrange the visual results in three categories, good, moderate, and failure, we have—perfect, 41 cases; moderate, 1 case; failure, 2 cases; vision not tested, 8 cases. In other words, out of these fifty cases only two failed to obtain sight. The main essential in this operation is absolute smoothness and exactness in the steps of the operation. Freedom from any hitch whatever is after all the best guarantee for sight restored. This, I think, is especially true in the simple extraction.

I think it is apparent that had simple extraction been generally adopted in this series of cases there would have been numerous prolapses of the iris; and while I am not disposed to lay as much stress on the gravity of a prolapsed iris as many seem to do, it is too early in the day to pass judgment, for an incarcerated portion of the iris, even if it does not give rise to immediate trouble, may do so many years later. And the very imperfect after-treatment which was the lot of the majority, while it shows that it is possible to get good vision with virtually no treatment after the operation, it ought not to prove that our hospital methods are attended with needless restrictions and that more freedom to the patient is quite as safe.

When a patient tears off the bandage and releases himself from all restraint on the third day after the operation, it is a very rare exception that any sight is restored, though there are few of us who have not had one or two just such cases and where most excellent vision was gotten. But such occurrences prove nothing, and they should not induce us to relax our care in the after-treatment of cataract patients, nor lead us to think that we can afford to allow our patients all sorts of liberties as soon as the operation is done.

I append herewith a tabular statement of each operation:

| No. | Sex. Age. Health. | Cataract. | Operation. Healing Process. Duration of Treatment. | Primary Vision. | Secondary Operation after Extraction. Duration of Treatment. | Ultimate Vision. | Remarks. |
|---|---|---|---|---|---|---|---|
| 1 | Male. 65. Good. | Hard. Ripe. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/30 | | | With iridectomy. |
| 2 | Male. 77. Good. | Hard. Ripe. Left Eye. | Patient jumped and dislocated lens into anterior chamber. Removed with difficulty. Mild iritis followed. Recovery in four weeks. | 20/100 | Discission one year later. Three days. | 20/40 | With iridectomy. |
| 3 | Female. 66. Rheumatic. | Hard. Ripe. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/70 | ..... | .. | With iridectomy. |
| 4 | Female. 60. Good. (Colored.) | Hard. Ripe. Right Eye. | Smooth. Slight hernia of iris, which was clipped off on third day. Recovery in sixteen days. | 20/40 | ..... | .. | Simple extraction. |
| 5 | Female. 66. Good. | Hard. Ripe. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/40 | ..... | .. | Simple extraction. |
| 6 | Female. 68. Diabetic. | Hard. Ripe. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/70 | Discission one year later. Three days. | 20/30 | With iridectomy. |
| 7 | Male. 75. Good. | Hard. Ripe. Right Eye. | Exposure brought on iritis on third day, and almost closed pupil was result. Three weeks. | 15/200 | Two years later, a triangular piece of iris removed over site of old iridectomy and iridotomy performed. Two weeks. | 20/70 | With iridectomy. |
| 8 | Male. 87. Asthmatic. (Colored.) | Hard. Ripe. Right Eye. | Some loss vitreous. Uncomplicated. Two weeks. | 20/50 One month later. | ..... | .. | With iridectomy. |
| 9 | Female. 55. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/100 | Discission six months later. Three days. | 20/40 | With iridectomy. |
| 10 | Male. 64. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/30 | ..... | .. | Simple extraction. |
| 11 | Male. 57. Rheumatic. | Hard. Left Eye. | Smooth. Slight prolapse of iris. Clipped off fourth day. | 20/100 | Discission four months later. Four days. | 20/30 | Simple extraction. |
| 12 | Female. 58. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/70 | ..... | .. | With iridectomy. |
| 13 | Female. 75. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/70 | ..... | .. | With iridectomy. |

| No. | Sex. Age. Health. | Cataract. | Operation. Healing Process. Duration of Treatment. | Primary Vision. | Secondary Operation after Extraction. Duration of Treatment. | Ultimate Vision. | Remarks. |
|---|---|---|---|---|---|---|---|
| 14 | Female. 60. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/30 | ..... | .. | With iridectomy. |
| 15 | Female. 68. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/30 | ..... | .. | With iridectomy. |
| 16 | Female. 71. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/100 | Discission eight months later. Three days. | 20/20 | With iridectomy. |
| 17 | Female. 71. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/70 | Discission three months later. Three days. | 20/40 | With iridectomy. |
| 18 | Female. 54. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 5/200 | ..... | .. | Patient had atrophy of optic nerve. |
| 19 | Male. 70. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/100 | Discission two months later. Three days. | 20/20 | With iridectomy. |
| 20 | Female. 77. Rheumatic. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/70 | ..... | .. | With iridectomy. |
| 21 | Female. 78. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/40 Four weeks later. | ..... | .. | With iridectomy. |
| 22 | Female. 78. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/50 Four weeks later. | ..... | .. | With iridectomy. |
| 23 | Female. 67. Asthmatic. | Hard. Right Eye. | Attack of asthma, and escape of vitreous. Five weeks. | 20/100 | ..... | .. | With iridectomy. |
| 24 | Male. 78. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/70 | ..... | .. | With iridectomy. |
| 25 | Female. 71. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/100 | Discission three months later. Four days. | 20/30 | With iridectomy. |
| 26 | Female. 75. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/30 | ..... | .. | With iridectomy. |
| 27 | Female. 72. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/40 | ..... | .. | With iridectomy. |
| 28 | Male. 52. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/100 | Eighteen months later. Three days. | 20/40 | The cataract was secondary to old iritis and the pupillary margin was bound down at one point. |
| 29 | Male. 53. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/70 | One year later. Three days. | 20/40 | Remains of several old adhesions. |
| 30 | Female. 69. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/50 | ..... | .. | With iridectomy. |
| 31 | Male. 76. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/100 | Three months later. Four days. | 20/20 | Preliminary operation (Förster) was here performed. |
| 32 | Male. 66. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/40 | ..... | .. | With iridectomy. |
| 33 | Male. 79. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/70 | Six months later. Three days. | 20/30 | With iridectomy. |
| 34 | Female. 72. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | 20/50 | One year later. Three days. | 20/30 | With iridectomy. |
| 35 | Female. 73. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/40 | ..... | .. | With iridectomy. |
| 36 | Female. 65. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/30 | ..... | .. | With iridectomy. |
| 37 | Male. 72. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/40 | ..... | .. | With iridectomy. |
| 38 | Female. 71. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | 20/50 | ..... | .. | With iridectomy. |
| 39 | Male. 91. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | Not taken. | ..... | .. | With iridectomy. |
| 40 | Male. 57. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Ten days. | Vision not taken. | ..... | .. | Simple extraction. |

| No. | Sex. Age. Health. | Cataract. | Operation. Healing Process. Duration of Treatment. | Primary Vision. | Secondary Operation after Extraction. Duration of Treatment. | Ultimate Vision. | Remarks. |
|---|---|---|---|---|---|---|---|
| 41 | Male. 37. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | Vision not taken. | ..... | .. | With iridectomy. |
| 42 | Male. 30. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | Not taken. | ..... | .. | With iridectomy. |
| 43 | Male. 77. Feeble. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | $\frac{20}{200}$ | ..... | .. | With iridectomy. Incipient atrophy. |
| 44 | Male. 12. | Traumatic. Left Eye. | Smooth. Uncomplicated. Two weeks. | Not taken. | ..... | .. | The cataract was a result of concussion. The lens was extracted without iridectomy. |
| 45 | 61. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | Not taken. | ..... | .. | ..... |
| 46 | Male. 21. Good. | Hard. Left Eye. | Smooth. Uncomplicated. Two weeks. | $\frac{20}{200}$ | ..... | .. | Discission. |
| 47 | Male. 61. Rheumatic, Varicose veins. | Hard. Left Eye. | Smooth. Twenty minutes later. Hemorrhage from within eye. | | ..... | .. | With iridectomy. |
| 48 | Male. 74. Good. | Hard. Right Eye. | Smooth. Uncomplicated. Two weeks. | Not taken. | ..... | .. | With iridectomy. |
| 49 | Female. 78. Good. | Hard. Left Eye. | Smooth. Lachrymal abscess gave rise to suppuration and eye was lost. | | ..... | .. | With iridectomy. |
| 50 | Male. 91. Good. | Hard. Left Eye. | ..... | Not taken. | ..... | .. | With iridectomy. |

# A CASE OF ASSOCIATED STREPTOCOCCUS INFECTION OF THE VERMIFORM APPENDIX AND FALLOPIAN TUBE.

BY HUNTER ROBB, M. D., *Associate in Gynecology to the Johns Hopkins Hospital, Baltimore, Md.*

HISTORY OF CASE.—N. D., aged 21, black, admitted to the Gynecological Ward of the Johns Hopkins Hospital, Nov. 4th, 1891. Married three years; mother of two children now two and one years of age; two miscarriages at seven and three months. Labors difficult, followed by fever. Menstruated at fifteen; during the past four months, menstrual periods every two weeks, lasting three days. Last period 20th of October, pale in color and slight in amount. Has had profuse leucorrhea for past two weeks. Bowels regular; no urinary trouble.

Complains of pain in side and back, headache and general weakness. Appetite good; tongue clean; body well nourished; no history of any serious illness.

Examination Nov. 7th, under ether: vaginal outlet moderately relaxed, cervix in the axis of the vagina, enlarged and soft, with a small bilateral laceration. External os patulous, admitting the tip of the index finger. Uterus reclining in the pelvis, enlarged and movable. Irregular tumor mass adherent to the broad ligament on the left side, about the size of a lemon. This adherent mass is semi-fluctuant, and of a doughy consistency; it displaces the uterus to the right. Right ovary high up in the pelvis, enlarged and adherent to the uterus.

*Per rectum:* adherent mass outlined on the left side. The tube and ovary on the right side are not distinctly palpated.

Abdominal section for the removal of adherent tubes and ovaries was advised.

Urinary analysis, Nov. 5th, 1891, catheterized specimen: clear amber color, sp. gr. 1.024, reaction acid, no albumen, mucous sediment. Moderate number of large epithelial cells, leucocytes free and in groups. Crystals of oxalate of lime. Catheterized specimen examined Nov. 11th; a trace of albumen with nitric acid on boiling. Slight mucous sediment.

*Operation, Nov.* 11th.—Patient prepared as usual; incision in the median line through moderately thick abdominal walls. The tube and ovary on left side were adherent to each other, and to the broad ligament and posterior surface of the uterus by dense connective tissue adhesions. The adhesions were so firm that it was impossible to enucleate this mass without rupturing the sac, which allowed several drachms of a purulent fluid to escape into the pelvis. Cultures were immediately taken from this escaping fluid. The tube and ovary were transfixed, incised, and the pedicle cauterized. The right tube and ovary were separated from the adhesions which bound them to the pelvic wall. The tube was elongated, thickened and patulous at the fimbriated extremity. The ovary on this side was also enlarged, and studded here and there with inflammatory patches from three to six mm. in diameter. The tube and ovary were transfixed and incised after the broad ligament was quilted by a series of silk ligatures and the pedicle cauterized. Before removing the right tube and ovary, the vermiform appendix was examined and found enlarged and adherent to the upper surface of the ovary. This was separated from the ovary; the lower portion for a

distance of 2 cm. was congested, thickened and covered with flakes of lymph. The mesappendix was well developed. After transfixing and incising the mesappendix, 4 cm. of the appendix was ligated by a circular suture to avoid penetrating the lumen of the appendix, which was then burnt off by Paquelin's cautery.

The peritoneal cavity was irrigated with four litres of a sterilized salt solution at a temperature of 112° F., and sponged dry. Owing to the separation of the large adherent surfaces, slight oozing persisted. The peritoneal cavity was closed by uniting the peritoneum with a continuous cat-gut suture, and the musculo-cutaneous surfaces with silk sutures. No drainage. Time of operation, fifty minutes.

The pulse immediately after the operation was full, regular, and strong.

*Cultures and smear preparations made from the right Fallopian tube and vermiform appendix immediately following the operation were pure cultures of the streptococcus pyogenes. Cultures taken during the operation from the pus which came from the left tube were negative.*

*Macroscopical examination of specimens removed.*[1]—They consisted of the Fallopian tubes and ovaries of both sides and a portion of the vermiform appendix.

Right side—Fallopian tube 10×.7×1.2 cm. Fimbriated end of the tube free; a few adhesions on the superior surface of the tube. 2.5 cm. from the fimbriated extremity there is a projection 5 mm. in diameter and 5 mm. high; this is probably a beginning supernumerary ostium. The tube is soft, red and swollen.

Ovary—5.5×3×1.5 cm. Few adhesions. The surface of the ovary is studded with many dropsical follicles, one at its lateral end being 2 cm. in diameter.

Left side—Tube 7×.3×2 cm. The fimbriated extremity is reddened and open. There are many dense adhesions; tube torn open during operation.

Ovary—4×2.5×1 cm. Attached to it are many adhesions. Ovary torn at pedicle.

Vermiform appendix. The appendix is represented by a mass of tissue 9 cm. long and 7 mm. in diameter, with a central lumen. It is covered by tolerably dense adhesions.

A segment of a tape-worm 15×14 mm. was forced out of the cut end on pressure. The free extremity of the appendix is covered with flakes of lymph.

*Analysis of temperature chart.*—For six days previous to the operation the temperature was 99° F. by the mouth (100.3° F. by the rectum). On the evening of the day of the operation it rose to 101.7° F. by the rectum, 100.2° F. by the mouth. On the second day it decreased to 100.8° F. by the rectum and 100.3° F. by the mouth. From this time it gradually but progressively rose to 105° F. by the rectum on the third day at 6 P. M. Pulse at this time was 130. At 8 P. M. on the same day the temperature registered 105.4° F. by the rectum. On the fourth day at 2 A. M. it registered by the axilla 105.8° F., and at 8 P. M. the axillary temperature was 103° F., the rectal 103.9° F. At midnight of the fourth day it was 104.4° F. by the axilla and 102.4° F. by the rectum. It then fluctuated between 103° F. and 104° F. by the axilla. The axilla temperatures that are recorded were registered after the thermometer had been in the axilla for twenty minutes.

The pulse varied from 120 to 140, most of the time being below 135. The morning of the fifth day it suddenly increased to 140 and remained between this and 130 until 10 A. M., when it again rose to 150 and afterwards to 180, when she died at 4 P. M.

She was stimulated by hypodermics of strychnia and digitalis; stimulants were also administered by the mouth and rectum.

Her bowels were fairly well opened by salts and oil enemata on the third day.

*Autopsy* made November 15, 1891, at 9 P. M., five hours after death.[1]

*Anatomical diagnosis.*—Intestinal hemorrhage, round ulcer of the duodenum, with erosion of small vein. Operation wound, removal of ovaries and tubes, amputation of appendix, localized peritonitis in pelvis and around stump of appendix; tape-worm in intestines.

All the tissues are very anæmic.

*Body.*—Large, strongly built, well nourished, no œdema, skin smooth, abundant fat in subcutaneous tissue, small amount of blood escapes on section. In anterior abdominal wall in the median line, commencing 4 cm. below navel, is an incision closed by sutures, the whole covered over tightly by a plaster sprinkled with iodoform. Edges of wound adherent. A slight amount of bloody exudation in and around the edges. Subcutaneous tissue and muscle on either side of wound contain a small amount of hemorrhagic infiltration.

On opening the abdominal cavity several loops of small intestines are distended and of a purplish color; the abdominal wound is slightly adherent to tissues beneath. The intestines are generally not adherent, but two or three loops of small intestine are lightly adherent in the pelvis. On separating these adhesions the adherent portions are covered by a slight hemorrhagic fibrinous exudation. The peritoneum is moist. In the pelvis, and partly shut in by adherent loops of intestine, there are about 50 cc. of hemorrhagic purulent fluid. Scattered over the intestine, especially over the most distended portions, there are a few very slight fibrinous flakes. A loop of the ileum is adherent at the end of the cæcum, and shut in by this adherent loop and by its own mesentery and by the peritoneum is a small cavity about as large as the end of the thumb, in which the cut end of the vermiform appendix appears ligated and bathed in a slight amount of pus. The cavity contains a small amount of hemorrhagic pus. The tubes and ovaries are removed, their stumps adherent to contiguous tissues. There are small coagula adherent to the wound surfaces. There are fresh adhesions between the uterus and rectum, and in the cavity so formed there is a small amount of soft coagulated blood.

*Diaphragm* on right side at lower border of fourth rib, on left at fifth intercostal space.

*Lungs.*—Both lungs free from adhesions; surfaces pale, bronchi pale, blood-vessels at root of lungs free, lungs œdematous, and scattered through them are small hemorrhagic

[1] The description of the specimens was made by Dr. J. Whitridge Williams.

[1] From the Pathological Laboratory of the Johns Hopkins Hospital.

foci, apparently about bronchi. In both bronchi there are aspirated hemorrhagic stomach contents. On posterior surface of left lung there are a few very small ecchymoses.

*Heart.*—Both layers of pericardium smooth. Heart firmly contracted, pale; valves normal. Thickness of firmly contracted left ventricle, 17 mm.; of right, 4.5 cm. Mitral orifice 8, tricuspid 10.5, aorta 5.5 cm.

*Liver.*—Free from adhesions. Exceedingly pale, of a whitish yellow color; on section little or no blood can be squeezed from it. Barely sinks in water; weight 1700 grams, 27×20×7 cm. Its surface covered with a few reddish specks.

*Spleen.*—10×7×3.5 cm. Weight 110 grams. Smooth; capsule tolerably tense. On section rather soft. Malpighian bodies increased.

*Kidneys.*—Left somewhat larger; both with pelvis slightly turned to front. Weight of both 330 grams. Fœtal lobulations well marked, especially on left kidney. Capsule easily stripped off. Surface of kidney rather pale; lobules well marked out. On section, of a light pinkish color. Structures normal. Cortex 1 cm. Pyramids extremely pale.

*Adrenal glands* and *pancreas*, normal. *Uterus* rather large, 8.5 cm. long. In fundus a somewhat hemorrhagic fluid.

*Intestines.*—In the entire large and small intestine there are large quantities of soft coagula, the quantity estimated at about three litres. The mucous membranes of small and large intestines normal. In the stomach there is also a considerable amount of blood. In the duodenum, on the posterior wall 5 mm. from the pylorus, there is a circular, slightly depressed ulcer 18 mm. in diameter, the edges towards the stomach more elevated and sharper than the remaining portion; surface of ulcer smooth. Muscular striation not visible. Adherent to its base there is a soft clot 6 cm. long. This clot apparently extends from a small eroded vein about 1 mm. in diameter in the base of the ulcer. There is a slight amount of bloody mucous fluid in the trachea. Cover-slips made at autopsy from the foci of local peritonitis give numerous streptococci. In the small intestines there is a completely formed tape-worm, which extended from the beginning of the jejunum throughout the entire lumen. (Tænia medio-canellata.) The microscopic examination of the liver shows a most intense fatty infiltration. Cover-slips at autopsy from the foci of peritonitis give numerous streptococci. These were not found in the peritoneum generally.

*Bacteriological examination.* (The cultures are either roll agar or stab agar.)

1. Roll agar of iliac veins (may have been contaminated) contains about 200 small, grayish-white colonies, resembling streptococcus colonies. Microscopically they are streptococci. In addition, fluid at the bottom of the tube contains some bacilli, some with unstained ends indistinguishable from bacillus coli communis. There are two colonies of a white or slightly yellow color, larger.

2. Slanting agar of heart muscle is sterile.

3. Slanting agar of lung is studded with colonies. The majority are minute and grow like streptococcus colonies. In addition there are about 100 yellow colonies. The former are all streptococci. The latter are typical staphylococcus pyogenes aureus; no other bacteria in fluid at bottom of tube.

4. Slanting agar of spleen sterile.

5. Slanting agar of kidney shows a slight whitish growth of a streptococcus at a point where needle has stabbed agar; none elsewhere. Roll agar from kidney is diffusely washed with a whitish-gray growth. In addition there are at least a dozen small white colonies of streptococcus. Fluid at bottom also shows streptococcus and some coarse bacilli, growing in chains of a dozen or more, much thicker and larger than colon bacilli, and probably representing some contamination.

6. Slanting agar of liver, tube broken and contaminated.

7. Roll agar of bile. One large, peculiar, white, irregularly spread out colony, and three small white colonies about 0.5 mm. in diameter. These are of a coarse irregularly staining bacillus, probably a contamination.

8. Roll agar from exudate in adhesions between loops of small intestines, and uterine stump studded with white colonies of streptococcus. In addition there are about twenty or thirty colonies of staphylococcus pyogenes aureus.

9. Roll agar from peritoneal fluid at a distance from preceding, about a dozen colonies of streptococcus showing that peritoneal infection was chiefly confined to the neighborhood of the stump.

10. Slanting agar from surface of loops of intestines shows no growth.

The case is interesting in showing a limitation of streptococcus peritonitis, perhaps due to absence of drainage tube.

## CONCLUSIONS.

The case is a very unique and interesting one in several aspects, and suggests many important considerations.

*First.* The unusual condition of pyosalpinx of one side with appendicitis, salpingitis and ovaritis of the opposite side, both the right tube and appendix containing the streptococcus pyogenes.

*Second.* The duodenal ulcer as a possible sequela of the cauterization of the pedicles and appendix. The ulcer, though recent, appears to be rather too far advanced to be regarded as due to the operation, and there are no observations which show that gastric or duodenal ulcers follow burns of this character.

***That the death was immediately due to the hemorrhage from the ulcer is clearly shown by the anæmia of all the tissues, the large amount of blood in the intestines, and the eroded vessel in the ulcer.***

*Third.* The presence of the segment of a tape-worm in the intestine and vermiform appendix, which might possibly have acted as a foreign body and had some connection with the appendicitis.

*Fourth.* Although it cannot be definitely stated that the infection extended from the appendix to the tube, the presence of the streptococci in and about the appendix and in the tube on the same side, and its absence in the other tube, speaks for this view.

*Fifth.* It demonstrates the uselessness of a drainage tube in the presence of virulent organisms, which, on the contrary, would diminish the resistance of the tissues and do harm by its presence. In this case it would not have drained, as the greater portion of the purulent fluid was walled off from the peritoneal cavity, the infection being thereby limited, and not of itself producing the fatal issue.

# THE GOLGI SILVER STAIN WITH THE CENTRAL NERVOUS SYSTEM, AND ITS RESULTS; A COLLECTIVE REVIEW.

By H. J. Berkley, M. D.

*Read before the Johns Hopkins Hospital Medical Society, January 4, 1892.*

Though the silver method of staining the central nervous system dates back to the first publication of Golgi[1] in 1873, it attracted but little attention among the investigators into neural histology, until the later contributions of Golgi,[2] and separate works of the Spanish brothers Santiago and Peter Ramòn y Cajal[3] made their appearance in 1888–9.

These investigations of the brothers Ramòn seem to have been made in entire ignorance of the later works of Golgi, and have, therefore, a greatly increased confirmatory value; they also carry the histological details considerably further than the first observer.

Since 1888, besides the contributions of Golgi and Ramòn, a host of articles has arisen, mainly from the pens of the German writers, among whom may be mentioned A. Kölliker, His, Waldeyer, Flechsig, Lenhossek, Schrwald, Retzius, and the recently issued digests of Riese[4] and Waldeyer,[5] from which, in connection with the works of Kölliker,[6] this rescript is extensively drawn.

## METHODS OF PREPARATION.

The first silver method of Golgi has become what is now known as the long method. It consists in the immersion of small, thin pieces of the central nervous tissues for from 14 to 50 days, or longer, in Müller's fluid, or in two per cent bichromate of potassium solution, the concentration to be rapidly increased to five per cent, after which they are washed in a weak solution of silver nitrate for fifteen minutes, transferred to a 75 per cent solution, where they are to remain two to three days. The pieces then come into frequently changed 40 per cent alcohol, are cut moist, dehydrated in absolute alcohol, and cleared in creosote and turpentine, and finally mounted in dammar-lac without cover-glass.

[1] Commun. preventiva Gazz. Med. Ital. Lomb., T. VI., 1873.

[2] Golgi, Sulla fina Anat. degli Org. centrali del Syst. nervoso, 1886 (chief work).—Arch. per le scienche Med., 1880, IV., 21.—Commun falta al. terzo Congress freniatr. ital. Reggio Emelia 1880 et Arch. ital. per le Malatti nervose, 1881.—Commun f. alla Sezione anat. del. III. Congr. Med. in Genova, 1880.—Atti del IV. Congr. freniat. ital. tenuto in Voghera, 1883. La Cellula nervosa motrice.—Anat. Anzeiger, 1890, author's reference, the Spinal Cord, also list of own writings.

[3] P. and S. Ramòn y Cajal, Revist. trimestrial de Histologia normal et Path., 1888–9, 2-3.—Internat. Monatsch. f. Anat. u. Phys., 1889, Bd. VI., H. 4–5.—La med. Practic., 1889, No. 88.—Anat. Anzeiger, 1890, 3-4.—Trabajos del. Labor. anat. delle Fac. de Med. Barcelona, 1890.—Gaz. San. de Barcelona, 1890, II., No. 12.—Internat. Monatsch. f. Anat., 1890, H. 1.—Anat. Anzeiger, 1890, Nos. 20, 21, 22.

[4] Centralblatt f. allg. Path. u. path. Anat., No. 12, 1891.

[5] Deutsche med. Wochensch., 1891, No. 44 u. ff., und Sonderabdruck, Leipsic, Thieme, 1891.

[6] Zeitsch. f. wissensch. Zoologie, XXIX., 4, Art. Das Kleinhirn; LI., Art. Das Rückenmark; u. Anat. Anzeiger, 1891, Nos. 14–15, Medulla Oblongata.

In 1880 Golgi altered this procedure for what is now known as the rapid method. The portions of the cerebrum and cord are hardened in a mixture of two parts of a one per cent osmic acid and eight parts of a two per cent bichromate potassium solution, in which it is only necessary for the specimens to remain for two to three days, when they are to be treated with the silver solutions as in the above method. S. Ramòn y Cajal (1888–9) further modified the mixture into one composed of

| | | |
|---|---|---|
| Kalii Bich., | 3 | parts. |
| One per cent Osmic Acid Sol., | 25 | " |
| Aqua Dest., | 100 | " |

This solution gives the most satisfactory results, but should be used in not too small quantities and changed at least twice during the first day. All tissues should be hardened in the dark, the time varying for embryonic from 24 up to 48 hours, for older tissues from two to three days. After this hardening the tissues are washed for a quarter hour in a 25 per cent silver nitrate solution, and then go into the 75 per cent solution, where they remain from 36 to 48 hours. Kölliker recommends for further treatment that the tissues be laid in 40 per cent spirit, then cut with the free hand, or better, that they be placed for one hour in absolute alcohol, one hour in celloidin, then, after an hour or two to harden, they are to be cut with the Schanze microtome. The sections are then placed for a quarter-hour in creosote, then in turpentine, and are finally imbedded in zylol-balsam without cover-glass. More simple, and giving equally good results, is to carefully wash the preparations in running water, to remove, so far as is possible, the silver precipitate from the exterior, cut them on the freezing microtome, dehydrate in absolute alcohol, clear with oil of bergamot, and mount in zylol-balsam without cover-slip.

Various investigators have tried to overcome the objection to the disuse of the cover-glass (all preparations soon decolorize when it is used, the supposed cause being the irregular drying of the balsam causing a diffusion stream that carries off the silver precipitate [Samassa]),[1] the most satisfactory being that of Greppin[2] by the use of hydrobromic acid, but the details must be sought in the original.

With both the long and the short methods, the nerve-cells, with their protoplasmic processes and all non-medullated nerve-fibres, are colored a deep black, the neuroglia cells and their extensions a reddish brown, while the vessels assume more of a reddish cast. At times certain lymph spaces and a few medullated nerve-fibres are also colored. It is not yet fully decided whether the coloration depends on an impregnation of the cell bodies with the silver salt, or if it is simply an incrustation. Golgi, Ramòn and Kölliker hold to the first

[1] Zeitsch. f. wissensch. Mikrosk., Bd. VII., H. 1.

[2] Arch. f. Anat. u. Phys., Supplement Band, 1889.

idea. It is only certain that with the non-medullated fibres it is a true impregnation.

In order, the nerve-fibres color the easiest, then follow the protoplasmic processes, the nerve-cell bodies, the neuroglia cells and blood-vessels. Frequently preparations are obtained in which apparently all the fibres are colored alone, and not a single nerve or neuroglia cell is tinged.

The drawbacks to the method are that it frequently completely fails; that in no preparation are all the nerve elements equally and at the same time tinged; lastly, owing to the irregular stain, the relation of the different elements to each other does not appear. The irregularity of the tinging of the nerve processes and cells has, however, its compensating advantages, enabling one to trace the individual process, or axis cylinder, when otherwise it would be lost in the dense felt-work of processes and fibres.

The method gives the best results with embryonic tissues, but excellent preparations may be obtained from older animals, and from man.

### THE CEREBRAL CORTEX.

In this region the researches of S. Ramòn are the most profound and far-reaching. Following his works, there exist three essential ganglion cell types to distinguish: (1) the great pyramidal cells, (2) spindle cells, three-cornered, and polygonal cells in the outer layers, (3) deeper lying three-cornered or spindle cells. The large pyramidal cells have, as Retzius[1] has very recently shown, an extraordinary rich branching of the protoplasmic processes, which reach to the sub-pial limit.

In the outer layer of the cortex Golgi and his scholars Mantinotti[2] and Sala[3] have discovered certain relations of the endings of the protoplasmic processes to the glia and vascular system, substantiating the first-named author's theory that the protoplasmic branches are purely nutritive to the cell body. This connection is, however, not substantiated by Ramòn and Retzius. The extraordinary abundance of the protoplasmic processes, and their different course, occasions Retzius to interpose the question if in fact all the processes have a similar importance or meaning, and in what relation do they stand to the side branches of the axis-cylinder process. The function of the protoplasmic processes belongs even yet to one of the darkest points in the anatomy of the nervous system.

Flechsig, two years ago, determined that the side branches from the axis-cylinder processes finally became the axis cylinder of medullated nerve-fibres.

According to Ramòn, the nerve process of the great pyramidal cells have a three-fold course: 1. They turn into the axis cylinder of the longitudinal white fibres of the cortex; 2. They bend into the medullated callosal fibres, which, either crossed or uncrossed, proceed onwards. Of the deeper lying smaller cortical cells it has been shown, especially by Mantinotti, that their axis-cylinder processes pursue exactly the reverse course of those belonging to the pyramidal cells. After coming off, mainly from the basal cell end, they curve and run upwards and pass into the tangential fibres along the outer layer of the cortex. Into the same fibre band also curve the axis-cylinder process extensions of the more superficial lying cells. Very singular is the discovery of Ramòn in the cortex of the rabbit, that bi-bolar and three-cornered cells exist that have several nerve protoplasmic extensions. These spring from the protoplasmic arms of the cells, give off side branches, and run in the superficial fibre layer. He found only free-ending terminations to these nerve processes and their collaterals.

The medullated fibres are to be separated chiefly into two systems: a transverse, the callosal fibres, and a longitudinal. The longitudinal stand, as already mentioned, in especial relation to the large pyramidal cells; with the callosal fibres, other pyramidal cells, whose processes either remain on the same side or cross to the opposite hemisphere. Besides these, other longitudinal fibres cross in the C. callosum to the contralateral side and give off collaterals, which are lost in end arborizations, or the whole callosal fibres may end in the same way.

Ramòn draws attention to the like relation of the fibres in the anterior commissure of the spinal cord. Accordingly we again meet with the same relations that Golgi's investigations have shown in the spinal cord and cerebellum, the richly branched, never anastomosing cell prolongations, the nerve processes set with collaterals; the collaterals of the white substance; in the corpus callosum, for example, and the end brushes of the fibres.

The latest investigations of Haller,[1] Nansen,[2] Fusari[3] and Retzius (*l. c.*) support these results in the main. Haller especially coincides with Golgi, and ascribes with him a two-fold origin to the nerve-fibres, in one direct from the nerve processes of the ganglion cells (motor fibres), and in the other for the sensible roots, from a network of fine anastomosing branched processes of the entire assembled ganglion cells; and, thirdly, connection processes, which join directly one ganglion cell with another. In this last respect, among recent observers, Haller stands alone.

With Golgi, Nansen describes cells of the second type with free-ending branches. Contrary to Golgi, he finds in no place anastomoses between the branches of the nerve-fibres and the ganglion cell processes; besides, he departs in several very essential particulars from the physiological explanations of all the cited writers in so far that he sees in the ganglion cells only a nutritive apparatus—an extreme view—and the carrying of the reflexes, as well as by the psycho-motor and psycho-sensory conduction through the so-called His-fibre network, direct from fibre to fibre, without any involvement of an active function of the cell.

Retzius, in the crustacea, sustains the main points of these investigators. The ganglion cells are monopolar, with the exception of some in the abdominal cavity; and have a single prolongation (Stammfortsatz). From this chief prolongation the nerve-fibre extends, either running longitudinally in the central system, or, proceeding further, passes to the peripheral nerves.

[1] Verhandlung d. biologischen Vereins in Stockholm, 1891.
[2] Cong. Med. di Pavia, Seduta VI. Riform Med., Oct. 1887.
[3] Zeit. f. wissensch. Zoologie, Bd. 52, H. 1, 1891.

[1] Morphologisches Jahresbericht, Bd. 17, 1888, etc.
[2] Anat. Anz., 1888.
[3] Internat. Monatsch. f. Anat. u. Phys., 1889, p. 275.

### THE CEREBELLAR CORTEX.

The cerebellar cortex naturally is divided into three concentric layers, a central white core, surrounded by a granular layer, which is again surmounted by the molecular or gray layer that extends to the sub-pial limit.

From the central core stream out medullated fibres, a considerable proportion becoming the axis-cylinder fibres of the Purkinje cells (Kölliker), while others pass beyond, and end in the molecular layer. Besides these radial fibres there is a plexus of finer fibres crossing in all directions through the granular layer, having at their outer edge a band of tangential fibres. The existence of this plexus is denied by some, they maintaining a felt-work.

In the granular layer are larger and smaller cells of nervous nature. The nerve process of the former frequently does not come off directly from the cell body, but from one or the other of the processes; it ascends, according to Ramòn and Kölliker, into the molecular layer, and separates at a right angle into two longitudinal varicose fibres, that run between the protoplasmic processes of the Purkinje cells, and end free without arborization. This is probably due, however, to defect in the silver stain (Kölliker). The protoplasmic processes of these cells branch sparingly, and end in a thick bunch of short branches (Golgi, Ramòn, Kölliker).

The larger cells are differently shaped in different animals, and in number are inconsiderable. Their processes are richly branched, run partly in the molecular and partly in the granular layers. Their nerve processes possess numerous branches, which are, according to Ramòn, without medullary covering. Kölliker has recently succeeded in staining the granules, which he holds to be nervous.

By the long method, the Purkinje cell-processes are most beautifully stained. These protoplasmic processes are very richly branched, ascend to the sub-pial limit, when they turn downward (Kölliker). They possess no anastomoses, and are supposed to be only nutritive in function (Golgi). The axis-cylinder process gives off a few branches in its course through the granular layer.

The nerve cells of the molecular layer are likewise separated into larger and smaller, the former in general being situated in the deeper portion, the others in the more central portion of the layer. The last show the common form of multipolar cells; the others, on the contrary, show a very peculiar relation of the nervous process that Ramòn and Golgi discovered. This process runs transversely in the layer at a certain distance from the edge of the granular layer; beginning fine at the cell body, it soon broadens out in a peculiar manner, and gives off numerous processes at right angles to the parent stem, which descend, then branch into numerous terminal filaments that surround the Purkinje cells as with a loose-meshed basket-work (Korbzellen, Kölliker).

Their protoplasmic processes ascend to the outermost part of the molecular layer. Besides these Korbzellen, other cells from the granular layer likewise surround the bases of the Purkinje cells with a basket-work, so that they are enveloped on all sides by a fine felt-work of naked axis-cylinder extensions.

### THE MEDULLA OBLONGATA (KÖLLIKER).

Our knowledge of the finer anatomy of this portion of the central nervous system is derived solely from the work of Kölliker (Anat. Anz., Nos. 14–15, 1891). He has shown that the cerebral nerves in general, inclusive of the descending root of the trigeminus, and those fibres coming from the nucleus ambiguus, have the same relation to the nerves of origin as those of the anterior spinal roots. On the other hand, the sensible cerebral nerves end with free arborizations in the neighborhood of the so-called sensible nuclei. Therefore the true origin of the sensible nerves is to be sought in the extra-cerebral ganglia (petrosal, jugular, etc.). Branching of the root-fibres on their entrance into the medulla is to be seen, especially in the cochlea and vestibular nerves, as well as in the sensible portion of the vago-glossopharyngeus. Collaterals are to be found on all root-fibres of the sensible nerves. Besides the pyramidal and cerebellar lateral tracts, portions of the posterior and anterior columns seem to ascend cerebralwards without interruption.

The pyramidal columns give off fibres to all the motor nuclei of origin, which branch among the cells. In these nuclei also end numerous sensible collaterals which serve as reflex paths.

Many of the fibre tracts have collaterals. In the pyramidal columns they are comparatively seldom seen; in the crura ad pontem they have not been found.

The nerve cells of the medulla conform mainly to the I type of Golgi. To the present time Kölliker has not discovered any well marked ones of the II type. Side branches are given off from the axis-cylinder processes.

### THE SPINAL CORD.

No other observer has progressed with the silver method so far in the histology of the cord as Santiago Ramòn; others have followed him, confirming his results, or in some measure departing from him. Kölliker, on the other hand, has worked out the connections and relations of the elements in so complete a manner that other works are simply drawn from his original.

The essence of Ramòn's work is first a separation of the ganglion cells into groups, according to the course of the axis-cylinder processes. He distinguishes (1) nerve-root cells, that send out their nerve process into the axis cylinder of an anterior root fibre. In many animals these are sparingly branched, in the chicken branched more numerously. (2) Cells which, though belonging to all the groups of the horns, send their nerve processes through the anterior commissure to the opposite side, where they enter into relations with the longitudinal fibres of the antero-lateral columns, the relation being made by a T formed juncture, or through a simple bending into the fibres of the column. (3) Cells which, though equally belonging to all parts of the gray columns, send their nerve processes into one or several of the white fibres of the columns, yet without crossing the commissure. (4) Cells of the posterior horns, whose nerve processes become richly branched and correspond to Golgi's II type, and are, according to Ramòn, sensible. There are also to be included the cells of the spinal ganglia, and another variety of cell discovered by Lenhossek

and Ramòn, lying within the lateral tracts of the gray columns, whose nerve processes pass directly out through the posterior roots.

Further, Ramòn has found that the posterior root fibres from the spinal ganglion cells branch in T form, but at a slightly pointed angle Y, into a longitudinal ascending and a longitudinal descending branch. These branches form the entire mass of the posterior columns, and compose the columns of Goll as well as those of Burdach.

From these root fibres, as well as from the branches of the posterior columns, come off branches—collateral fibres—that pass into the gray substance and end in free arborizations. These collateral fibres comprise the hitherto called direct entering root fibres.

Collaterals analogous to those of the root fibres come off from all the other columns of the cord, and also end free in the gray substance.

The nerve process of a great number of the ganglion cells of all portions of the gray substance pass directly into the axis cylinder of a medullated fibre in the columns of the cord, and in the following manner: first they branch into two portions at right angles to the parent stem, this branching always taking place at one of the constrictions of Ranvier; secondly, they branch into two fibres, each being inserted into one of the constrictions of Ranvier of a longitudinal fibre. The nerve process may also bend directly into the axis-cylinder of one of the longitudinal fibres. This is especially the case with the cells of Clarke's columns, whose processes coursing cerebral-wards, bend upward to enter the lateral cerebellar tract.

The collaterals of the antero-lateral columns are the largest and best developed, their arborizations lie among the cells of the anterior horns, a part of them also cross in the anterior commissure. The collaterals of the posterior columns are fine, very numerous; part of them end in the region of the anterior horns, a part cross in the posterior commissure and end partly in the posterior horn, partly in the anterior horn of the opposite side. Of the endings of the parent stems of the longitudinal fibres nothing positive is known. One parent stem may give off many collaterals, whose arborizations surround ganglion cells and directly influence them.

Following the ideas of Kölliker, the conduction of the nerve impulses through the cord is the following:

(1). The fibres of the pyramidal columns and their collaterals enter into the gray substance, surround the motor cells with arborizations, excite them through contact, the excitation being continued through the medium of the cell to its motor root fibre, which then continues it to the muscular or epithelial termination.

(2). The conscious sensations are conducted through a portion of the posterior root fibres, then to the posterior columns, thence to the medulla.

(3). The reflexes are explained through the collaterals of the sensible fibres surrounding the motor cells, and through contact exciting them, thence the excitation is propagated along the motor nerve fibre. The motor cells are thus surrounded by two sets of terminal arborizations, from the pyramidal fibres and from the branches of the sensitive roots. Crossed reflexes are explained by the presence of numerous axis-cylinder processes, which extend from one side to the other of the gray columns through the commissure, and excite the motor cells of the opposite side.

General reflex movements, as of the decapitated frog, are explained in a twofold manner, either through the property of the sensible fibres giving off through their entire course collaterals, so that one fibre may influence quite distant tracts on the cord, or through the action of the sensible collaterals on the cells of the columns, which on their part influence the endings, and the collaterals of their axis-cylinder processes carry over the irritation to nearer or further lying motor cells of the anterior and lateral columns of the same or opposite side. The end station of the sensible fibres must be sought for partly in the medulla, partly in the cerebrum and cerebellum.

### THE GLIA ELEMENTS.

The work that has been done in this department of the central nervous system has been principally by Lenhossek,[1] S. Ramòn,[2] Kölliker,[3] Retzius,[4] Oyarzun,[5] Lavdowski,[6] and Rohde.[7]

The general result of their work is to divide the glia proper into two divisions: that coming from the ependyma of the ventricles and central canal, and another variety corresponding to the spider cells of Deiters.

Furthermore, in the brain the second variety is subdivided by some differences in the shape of the cells into a peripheral and a deeper lying variety. These have in extra-uterine life no dependence on the ventricle epithelium, though, according to Lenhossek and Ramòn, they are originally derived from the ependymal cells. Ramòn asserts this with positiveness for all animals, Lenhossek for the chicken only, the latter's researches being with embryos of the 6th day, when the connection is evident.

The Deiters cells show nowhere anastomoses of the extensions, and are very numerous in the sub-pial layer and in the white substance, less abundant among the cellular layers. The ependymal glia begins at the ventrical wall with long-branched ramifications, which extend through the entire thickness of the brain and cord. Their nuclei lie close to the ventricle wall, and the peripheral portion makes its termination in a knob-shaped ending in the sub-pial layer.

An undecided question is whether in after-life other connective tissue elements are not associated with the ectodermal glia. Ramòn considers it probable; Rohde distinguishes with a class of the invertebrates (Hirndineen) two varieties of supporting substances; one originating from cells of ectodermal origin, as the nerve elements themselves, the other a true connective tissue element.

### RESULTS.

The chief results of the investigations of Golgi, Ramòn, and Kölliker, with the confirmatory support of numerous other observers, have been: (1) the discovery of the so-called col-

[1] Verhandlung d. Anatomen Versammlung in München, 1891.
[2] Anat. Anz., 1890, Nos. 4-20. [3] L. c., Das Rückenmark.
[4] Verhand. d. biologischen Vereins in Stockholm, 1891.
[5] Arch. f. mik. Anat., Bd. 35, 1890. [6] Ibid., 38, H. 2, 1891.
[7] Untersuch. an d. Nervensyst. d. Hirndineen, Schneider, Breslau, 1891.

laterals, branches, that are given off from the nerve fibres through every part of their course in the central system; (2) that these collaterals end in fine brushes (arborizationes finales, S. Ramòn; Endbaumchen, Kölliker) that enclose the nerve cells as in a basket of fibres, and act upon them by direct influence, possibly; (3) that many collaterals may be given off in the course of a single nerve fibre, and that one fibre may thus influence a large number of nerve cells; (4) that every fibre originates from a single cell; (5) that the fibres of the posterior roots of the cord are in conjunction with fibres that come from the spinal ganglia, and that these fibres, after passing inward, branch in T form, one portion of which ascends in the posterior columns, the other descends; and that from the root fibres themselves, as well as from both longitudinal branches, come off side branches which enter directly into the gray substance, there ending free with arborizations. Finally, for the fibres, their peripheral terminations end free in wide spread out brushes; for example, in the epithelium and muscles, the latter being in connection with the end plates.

The centripetal terminations of all nerves and collaterals are held by Ramòn to end with free branching in the gray substance; Golgi holds that they end in a diffuse network.

Golgi divides the ganglion cells into two chief varieties, motor and sensible. The first are differentiated by the presence of a single axis-cylinder process, which gives off fewer branches than the other cell processes, and finally passes into the axis cylinder of a medullated nerve tube. The second variety are distinguished by the axis-cylinder process being shorter than in the motor, and by its subdividing equally with the other processes, until they end within the gray substance in a fine felt-work of processes.

There is some doubt, however, on this point, Golgi maintaining a network, Ramòn a felt-work, the only certain point being that they end in fine filaments.

Further, the protoplasmic processes branch in a hitherto unknown fineness; anastomoses are not to be found between the separate processes of a cell, or between those of different cells, and such anastomoses are said never to occur (Ramòn).

The protoplasmic processes are considered to be of non-nervous nature by the majority of investigators, Ramòn dissenting from this view, and are supposed to have solely a nutritive function. Golgi has discovered connections between the blood-vessels and glia cells with these processes, a result that is unconfirmed by any other observer.

In accordance with these ideas, the so-called law of isolated conduction has every anatomical support withdrawn, and is no longer tenable, so far as the anatomy and functions of the ganglion cells and their connections can be shown.

In conclusion, for the nervous system—following Waldeyer—it may be said to consist of very numerous, anatomically as well as genetically, separate nerve entities. Each nerve-entity consists of three portions, the nerve cell, the nerve fibre, and the end arborization. The physiological conduction may proceed equally well from the cell to the end-brush, or from the end-brush to the cell. Motor conduction proceeds only from the cell to the end-brush, the sensible sometimes in one, sometimes in the other direction.

The researches in the neuroglia structures of the cord and brain have conclusively proven that the glia primarily results from the so-called epithelial cells of the ventricles and central canal, whose prolongations radiate through the entire cord and brain and end close to the pia. Later the epithelial extensions alter, become less and less distinguishable, and are replaced by a multitude of new glia cells, the well known spider elements.

The development of the nerve elements of the central system has been especially investigated by Ramòn y Cajal in the embryo of the chicken (Anat. Anz., 1890, Nos. 21, 22). From the third to the tenth day the epithelial cells of the primitive nerve elements (neuroblasts) alter, and show during their development three stages: the first an epithelial or bi-bolar, during which there is present a process to the central canal, and another to the periphery; later, there is a second or unipolar stage, in which the central process becomes stunted and disappears; lastly, the cell becomes multipolar, protoplasmic processes coming out from the cell body.

By the third day the cells of the anterior horns and anterior commissure develop, and almost simultaneously develop the anterior and posterior roots. Then, in order, follow the cells of the lateral columns, whose processes enter into the sensible roots, and shortly the remaining cells of the lateral columns and of the posterior commissure. On the fifth day the collaterals of the anterior columns make their appearance, followed on the seventh day by those of the posterior columns, and on the tenth day by those of the gray substance. Axis-cylinder, protoplasmic processes, and collaterals, show during their growth a conical swelling at their terminations.

# PROCEEDINGS OF SOCIETIES.

## THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

*Meeting of November 2d, 1891.*

Dr. HALSTED in the chair. 48 members present.

**Colles' Fracture.**—Dr. HALSTED.

In the absence of Dr. FINNEY, Dr. Halsted exhibited several cases illustrating the method employed in the treatment of Colles' fracture in the Hospital. The distinctive features of this method are the narrow, short anterior and loose posterior straight splints, with a pad under and against the styloid process of the ulna, in order to overcome the lateral and forward displacement so constantly observed in the so-called Colles' fracture of the radius.

**A Case of Glaucoma.**—Dr. THEOBALD.

Dr. THEOBALD reported a case in which a double needle operation upon an old, shrunken, traumatic cataract in a man thirty-one years of age was followed two weeks afterwards by the development of glaucomatous symptoms. The immediate cause of the glaucomatous attack seemed to be a slight blow upon the eye from a child's hand. The feature of interest in the case was that, after eserine had been used without effect, the glaucomatous symptoms were permanently relieved by atropia. This would not have been remarkable had there been swelling of the lens and consequent pressure upon the iris; but this was not the case, the iris not having been in contact with the lens at any time. The glau-

comatous condition, consisting of high tension and steaminess of the cornea, although varying somewhat in intensity, persisted, notwithstanding the local application of opium and eserine and the administration of biniodide of mercury, for two months. A single application of a four-grain solution of atropia was then made, with some misgivings, and was followed at once by an amelioration of the symptoms. After this a one-grain solution of atropia was applied once a day, and under this treatment and the continued administration of the biniodide of mercury the glaucomatous symptoms entirely disappeared at the expiration of four weeks. Subsequently a second needle operation was performed and $v = \frac{20}{\times 4}$ was obtained. The cataract was the result of a blow by a stone and had existed for fifteen years. The sight of the other eye was also defective, from lens opacity of traumatic origin.

**Aneurism with Demonstration of Bacilli causing air in Tissues.**—Dr. WELCH. [To appear in a future number.]

**Extra-Uterine Pregnancy.**—Dr. KELLY. [To appear in a future number.]

*Meeting of November 16th.*

Dr. HALSTED in the chair. 38 members present.

**Unusual Ulceration of Ileum.**—Dr. COUNCILMAN.

Dr. Councilman showed specimens of an unusual form of ulceration of the ileum. M. T., age 43, admitted into the Johns Hopkins Hospital November 21st; died December 10th. The patient had been married nineteen years, during which time she became pregnant six times, each pregnancy being followed by miscarriage. On admission she complained of pain in the rectum and constipation. This condition was first noticed two years previously, beginning with pain and burning sensation in the rectum. The formed stools are very small and voided with difficulty. At times there has been diarrhœa.

On examination, a stricture of the rectum was found which with difficulty admitted the tip of the index finger. On November 28 the stricture was dilated under ether. She reacted well after the operation. A few days afterwards she complained of violent pain in the rectum; vomiting began, which continued more or less until death.

*Autopsy.*—Body 150 cm. long, small, slightly built, emaciated; mucous membranes pale; lower extremities œdematous. Subcutaneous fat slight in amount.

The peritoneum smooth and moist. Several loops of small intestine are adherent to the pelvic organs, and on separating the firmest of these a small amount of pus welled up between the uterus and rectum. There are also a few adhesions of the small intestine to the mesentery, making sharp angles in the intestine at the point of adhesion.

There is nothing of any importance in the heart, lungs, trachea, liver, pancreas and adrenal glands.

The spleen is small—$9 \times 5 \times 2$ cm., and weighs 60 grams. On section it is smooth, pale; malpighian bodies not visible, trabeculæ faintly so.

Both kidneys present the same general appearance. The capsule is slightly adherent, the cortex somewhat roughened, pale and anæmic. On section the cortex is pale, slightly yellowish, with small areas more opaque than the rest. The striation slightly obscured.

The mesenteric and post-peritoneal glands are of normal size and firm.

The pelvic organs are intimately bound together in a mass of adhesions, and on separating these a small amount of yellowish pus appears. There is an extensive fissure of the cervix uteri. The ovaries and tubes are included in the pelvic adhesions and show no lesions. In the lower portion of the rectum there is a large ulcer or fissure, with hard, uneven, indurated edges. This opens into a cavity extending everywhere around the rectum and filled with black, gangrenous, stinking sloughs. There is purulent infiltration with formation of small abscesses around this, some of these abscesses extending into the pelvic peritoneum and shut in by the adhesions. There is a stricture of the rectum which extends from the anus to the end of the sigmoid flexure. The average circumference of the inner surface is 3.5 cm. The mucous membrane appears to be absent throughout its entire extent; the surface is pale and indurated. The muscle is much thickened, in some places measuring 6 mm., and from the thickened muscle dense bands of hard connective tissue extend into the surrounding fat.

The œsophagus, stomach and the upper part of the small intestine and the colon show nothing abnormal

Numerous ulcers are found over a region of the ileum commencing at a point one meter above the ileo-cæcal valve and extending from this 1.5 meters towards the stomach. The largest of these ulcers is nearest the stomach. It is immediately over a small adhesion of the intestine to the mesentery. This ulcer is almost perfectly round and is 18 mm. in diameter. The edges are sharp and slightly undermined. The base is covered with pale granulation tissue and is generally formed by the muscular coat. At two places, however, the ulcer extends through this, and is kept from perforation only by the adhesions mentioned above. There are other smaller ulcers similar in character to this large ulcer, some of them appearing to consist only of erosions of the mucous membrane; others penetrating through the muscularis mucosæ. These ulcers seem to have some tendency to occur in groups. The mucous membrane around them appears pale and somewhat softer than normal. In one place the mucous membrane is thickened, hyperæmic and covered with small ulcers which are not more than 2.5 mm. in diameter, the edges sharp and undermined, the base covered with a soft granulation tissue. They show no tendency to run together to form large ulcers. The peritoneum over all these ulcers is slightly thickened and opaque. None of these ulcers have any relation to the solitary follicles or Peyer's patches. There is no enlargement of the follicles in either the small or large intestine.

Frozen sections of the stricture show an entire absence of mucous membrane, the stricture being lined with a dense layer of granulation tissue, the cells of which are very fatty. This extends in the form of dense bands through the muscle and the surrounding indurated fat. None of the tissues are amyloid. The kidneys show slight fatty degeneration occurring in foci, and a marked cloudy swelling of the epithelium of convoluted tubules. There is a general diffuse formation of connective tissue with cellular infiltration principally around the glomeruli. Cultures made at the autopsy show colon bacilli in the lung, kidney, spleen and bile. Those made from the liver are sterile.

*Anatomical Diagnosis.*—Stricture of the rectum, with perforation and gangrenous periproctitis. Localized peritonitis. Ulceration of ileum, with invasion of the tissues by colon bacilli.

On examination of the ulcers in the ileum after hardening in alcohol, some were found to be of acute formation; others more chronic. The mucous membrane around those in which the process is more acute is somewhat swollen and infiltrated with granulation and pus cells.

There is necrosis of the surface, in some places only involving a part of the mucous membrane, in others extending through this and the muscularis mucosæ into the submucous tissue. The ulcers are lined with granulation tissue, the surface of which is necrotic. In some of the ulcers there are masses of pus cells extending deeply into the submucous tissue. Nearly all of them are undermined. The submucous tissue is swollen and infiltrated with granulation and pus cells, the infiltration extending widely from the ulcer. In places it extends down through the muscularis coats to the peritoneum. In the more chronic ulcers the cellular infiltration in the deeper layers is more marked. Around these there are no lesions in the mucous membrane.

Numerous bacteria, both short rods and micrococci, were found in the superficial necrosis, in some places extending into the cellular infiltration in the submucosa. They did not seem to stand in any etiological relation to the pathological changes.

The case is of interest as showing an acute inflammation of the small intestine which is neither typhoid nor tubercular in character and not connected with the follicles.

**Acute Ataxia following Diarrhœa.**—Dr. BERKLEY. [See January-February Bulletin, page 9.]

**Fifty Consecutive Operations for Cataract.**—Dr. RANDOLPH. [See page 19.]

**Lympho-Sarcomata.**—Dr. FLEXNER.

Dr. FLEXNER.—The case which we wish to report briefly to-night was admitted into the Hospital, in the service of Dr. Osler, on the 12th of August, 1891, and died on the 17th of August following. The patient, a man of 27, had been ill in all less than three months, and previous to his admission his prominent symptoms had been diarrhœa, painful micturition and rapid failing, added to which, at the time he came into the Hospital, was uncontrollable vomiting.

The autopsy, which was made by Dr. Welch a few hours after death, revealed, in brief, a number of depressed patches in the stomach, several tumors in the intestine, a general atrophic condition of the mucous membrane of the intestine, and a single tumor nodule in the liver. The kidneys were enlarged, the surfaces smooth, and they presented a distinctly mottled aspect, the ground being red, interspersed with grayish-white lines and patches.

The largest tumor of the intestine measured 2 cm. in length, parallel to the axis of the gut, and 3.5 cm. in width; it occupied a little more than one-half of the inner circumference of the gut. The growth projected a little way into the lumen; its central part was superficially ulcerated. Two other distinct tumors were situated above this one, and there were circumscribed areas in which the mucous membrane appeared to be thickened by an infiltration of the same material as composed the tumors. The tumor in the liver was situated in the right lobe and it measured 2.5 cm. in diameter; it was approximately spherical.

On microscopical examination the tumors proved to be lympho-sarcomata. The structure was like that of a lymphatic gland much hypertrophied, the distinction between lymph-nodules and lymph-sinuses having disappeared, and the trabecular framework of the glands had become much thickened and converted into dense bands of connective tissue. In the liver, the tumor was composed of lymphoid cells similar to those in the intestine, and it had originated in one or more portal spaces. The tumor cells are found surrounding the blood-vessels of the portal spaces, and in addition they have invaded the lobules themselves. Many lobules are completely obliterated by the growth of the tumor within them, and in others small islands of liver cells are separated from each other, owing to the extension of the tumor between them. Besides the tumor nodules just described there is a diffuse growth of a similar tissue in the intestine. Both processes, that is, the nodular and the diffuse, have taken place principally in the submucosa and mucous membrane. In the stomach a similar diffuse growth of the tumor tissue has occurred, especially in those areas spoken of as depressed; and in the kidneys the enlargement and mottling of them is due to the new growth of tumor cells. In the kidney the process had begun in the interstitial tissue between the tubules and surrounding the blood-vessels, and had gradually spread over the tubules and enveloped the glomeruli.

In the liver many of the liver cells had undergone fatty degeneration and some were hyaline and necrotic. There were fatty changes in the epithelium of the kidneys and a small amount of hyaline degeneration of epithelium. But in the stomach, and especially in the intestines, there was a very extensive degeneration of the structures of the mucous membrane, associated with atrophy. Several degrees of the degeneration and atrophy were present in the intestines, indicating a progressive process. The change in the mucous membrane was greatest in the immediate neighborhood of the nodules or close by, but it was very great also in those areas in which the diffuse process only was present, and it occurred even where no actual new formation of tumor cells had taken place.

It would seem as if there were a close relationship between the two processes, the diffuse and nodular developments of lymphoid cells within the organs and the degenerative and atrophic changes in the structures in which they have formed. It has been suggested, on histological grounds, that lympho-sarcomata probably belong to the infective granulomata to which tuberculosis, syphilis and typhoid fever belong; there is, besides, much clinical evidence in favor of such a classification of lympho-sarcomata, and if it is shown that the development of this process in tissues and organs can give rise to grave degenerative changes in them, it will afford additional support for such a view.

[A fuller report will appear in the *Johns Hopkins Hospital Reports.*]


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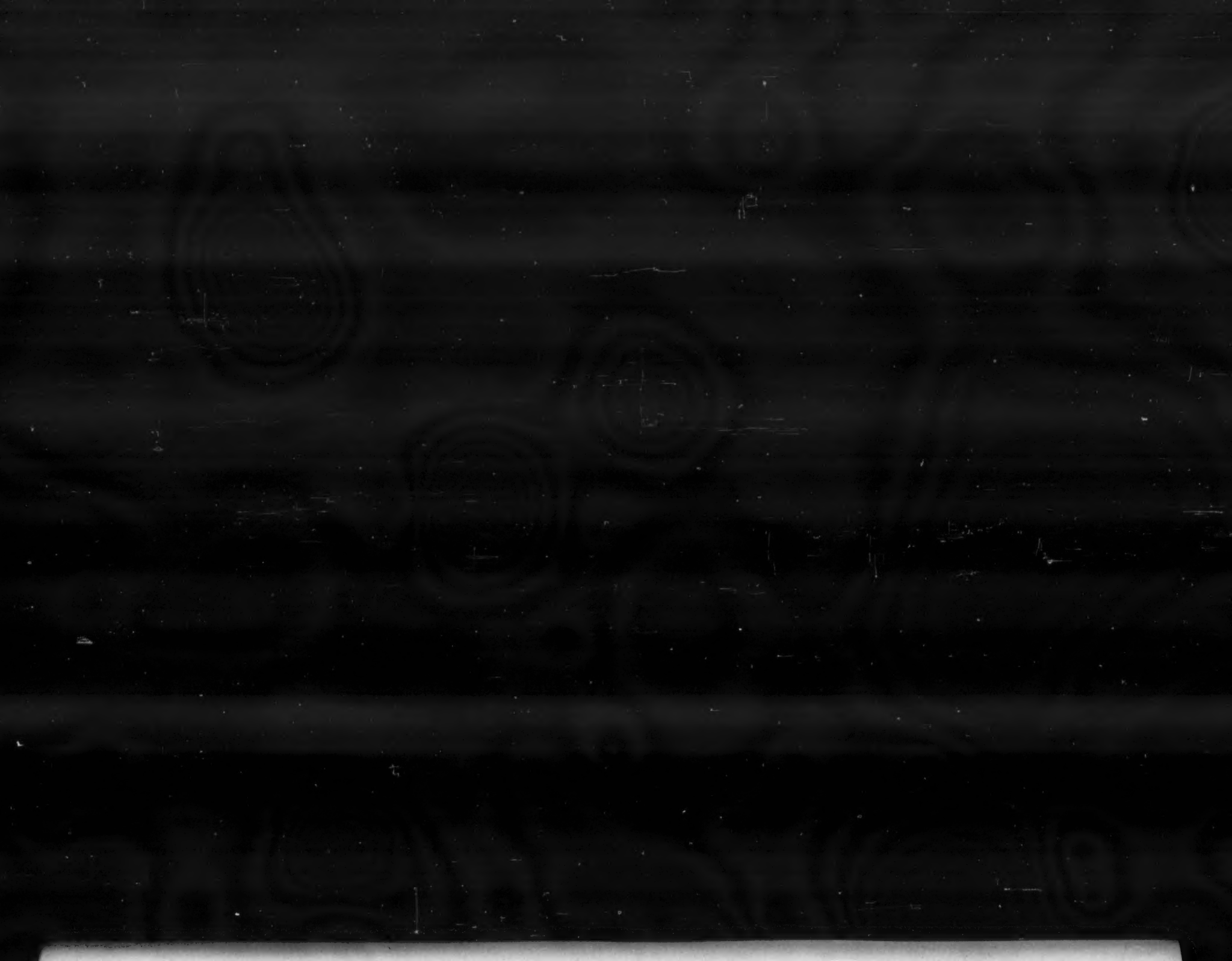
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